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REMARKS

Claims 1,5, and 12-30 are under consideration. Claims 1 and 29 have been amended. Four Office Actions have issued in this matter.

The Prosecution of the application is as follows:

1. 9/26/01—Office Action Restriction
2. 10/25/01—Response, Election
3. 3/27/02—Office Action
    a. Section 112, second paragraph, "micelles" and "emulsions"
    b. Section 102 (b)
        i. WO 88/00824
        ii. U.S. Patent No. 5,662,932 by Amselem
        iii. U.S. Patent No. 6,117,415 by Schwartz
    c. Section 103
        i. WO 88/00824
        ii. U.S. Patent No. 5,662, 932 by Amselem
        iii. U.S. Patent No. 6,117,415 by Schwartz
4. 6/20/02—Response
5. 10/10/02—Final Office Action
    a. Section 102 (b)
        i. WO 88/00824
        ii. U.S. Patent No. 5,662, 932 by Amselem
        iii. U.S. Patent No. 6,117,415 by Schwartz
    b. Section 103
        i. WO 88/00824
    c. 1.114
        i. U.S. Patent No. 5,662, 932 by Amselem
        ii. U.S. Patent No. 6,117,415 by Schwartz
6. 1/10/03 CPA-Amendment
7. 4/4/03 Office Action
    a. Section 112, first paragraph
    b. Section 112, second paragraph
    c. Section 102 (b)
        i. U.S. Patent 5,338,761 No. by Nakajima
        ii. U.S. Patent No. 5,376,646 by Pittrof
    d. Section 102 (e)
        i. U.S. Patent No. 6,117,415 by Schwartz
    e. Section 103
        i. U.S. Patent No. 5,376,646 by Pittrof
        ii. U.S. Patent No. 5,662, 932 by Amselem

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Rejection under 35 U.S.C. § 112, First paragraph

The Action rejects claim 1,5, and 12-30 as containing subject matter not described in the specification, for example:

- "Having no positively charged lipid but instead"
- "Having no phospholipid envelope or bioadhesive polymer coating"
- "The lipid carrier should not be a positively charged lipid"

In response, applicants have amended claims 1 and 29 to include limitations that distinguish the present invention from prior art cited, and have expressed support in the specification for example; 1) lipid carrier having high adhesive capability to mucosal membranes on page 4, line 3; and 2) lipid being characterized as mixed micelles on page 3, lines 9-11 and page 6, lines 14-19. This amendment should not result in a further rejection for the following reasons.

Applicants refer to a rejection made under Section 112, second paragraph, in the Office Action dated March 27,2002, in which the Examiner stated that,

"The distinction between a micellar dispersion and emulsion as recited in claims 1 and 29 is unclear. Micelles are emulsions since micelles of one phase are in suspension in another phase."

Applicants respectfully disagree with Examiner's statement, because it is factually wrong. This is because micelles are not emulsions, and applicants refer to the American Heritage College Dictionary, 3rd edition as authority to define the terms '*micelle*' and '*emulsion*'.

The definition of 'micelle' is, "*A submicroscopic aggregation of molecules, as a droplet on a colloidal system.*"

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The definition of emulsion is given as, *" A suspension on small globules of one liquid in a second liquid with which the first will not mix, e.g., an emulsion of oil in vinegar."*

The definition of colloid is *"A suspension of finely divided particles in a continuous medium in which the particles are approx. 5 to 5000 angstroms in size."*

It is clear from the above definitions that micelles are not emulsions. It is also clear that the Examiner's incorrect interpretation of the terms 'micelles' and 'emulsions' (made in the Office Action dated March 27, 2002) has resulted in the citation of other prior art during the prosecution of this application, for example:

- WO 88/00824
- U.S. Patent No. 5,662,932
- U.S. Patent No. 6,117,415
- U.S. Patent No. 5,338,761
- U.S. Patent No. 5,376,646

Applicant will not analyze these references at this point, but will discuss them below in reference to the pertinent rejections under different sections in light of the latest Office Action.

Claims 1,5, and 12-20 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite, for including two typographical errors; 1) 'ration' instead of 'ratio' and 2) 'bys' instead of 'by'. Applicant thanks the Examiner for pointing out these mistakes, apologizes for these informalities, and has corrected the two mistakes.

The Action points out that phosphatidylcholine chlorine (PC) and soya or egg lecithin are one and the same. Applicants agree that soya and egg lecithins contain

phosphatidylcholine chlorine. However, these lecithins also contain other lipids and applicants here used PC to represent the pure component.

The Action points out the use of the word 'gastrointestinal' as being indefinite. Applicants have used this word to describe the drug delivery at the gastrointestinal mucosa that one skilled in the art would interpret as the having reached this site via the oral route or directly through gastric intubation.

The following trade names have been used in the specification and their chemical names have been given here as well as in the amended claims:

Acetylsalicylic acid	2-acetoxybenzoic acid
Acyclovir	2-Amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-6H-purin-6-one
Amantadine	Cis-1-Acetyl-4-[4-[[2-(2,4-dichloro-phenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxo-lan-4-yl]methoxyl]-phenyl]piperazine
Amphotericin	Polyene antibiotic produced by Streptomycetes nodosus M4575
Ascorbyl palmitate	(S)-(+)-2-[(R)-3,4-Dihydroxy-5-oxygen-2,5-dihydrogen-2-furan]-2-ethoxyls cetane
Azothymidin	2-Amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-6H-purin-6-one monosodium salt
Benzocaine	4-Aminobenzoic acid ethyl ester
Biotin	cis-tetrahydro-2-oxothieno[3,4-d]imidazoline-4-valeric acid
Carnitine	3-Carboxy-2-hydroxy-N,N,N-trimethyl-1-propanaminium inner salt; (3-carboxy-2-hydroxypropyl)trimethylammonium hydroxide, inner salt
Cetylpyridinium chloride	1-Hexadecylpyridinium chloride
Chloramphenicol	D-threo-N-dichloroacetyl-1-p-nitrophenyl-2-amino-1,3-propanediol; D-)-(threo-2-dichloroacetamido-1-p-nitrophenyl-1,3-propanediol

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Chlorhexidine	N,N"-Bis(4-chlorophenyl)-3,12-diimino-2,4,11,13-tetraazatetradecanediimidamide; 1,1'-hexamethylenebis[5-(p-chlorophenyl)biguanide];
Coenzyme Q-50	
Dexamethazone	(11-beta ,16-alpha) 9-Fluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione
Diclofenac	[o-(2,6-dichloroanilino)phenyl]acetic acid sodium salt
Erythromycin	3-de[(2,6-dideoxy-3-C-methyl-3-O-methyl-.alpha.-L-ribo-hexopyranosyl)oxy]-11,12-dideoxy-6-O-methyl-3-oxo-12,11-[oxycarbonyl[[4-[4-(3-pyridinyl)-1H-imidazol-1-yl]butyl]imino]]
Flourometholone	21-desoxy-9alpha-fluoro-6alpha-methylprednisolone
Flucoconazole	1H-1,2,4-Triazole-1-ethanol, alpha-(2,4-difluorophenyl)-alpha-(1H-1,2,4-triazol-1-ylmethyl)- 2-(2,4-Difluorophenyl)-1,3-bis(1H-1,2,4-triazol-1-yl)-2-propanol alpha-(2,4-Difluorophenyl)-alpha-(1H-1,2,4-triazol-1-ylmethyl)-1H-1,2,4-triazole-1-ethanol
Indomethacin	1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetic acid
Ketoconazole	Cis-1-Acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]piperazine
Ketoprofen	(RS)-2-(3-benzoylphenyl) propionic acid
Lidocaine	omega-diethylamino-2,6-dimethylacetanilide
Lipoic acid	5-[3-(1,2-dithiolanyl)]pentanoic acid
Miconazole	1-[2,4-dichloro-beta-[(2,4-dichlorobenzyl)oxy [phenethyl]imidazole
Nystatin	2-Deoxy-4-O-(2,6-diamine-2,6-dideoxy-alpha-D-glucopyranosyl)-D-streptamine
Prednisolone	(11-beta)-11,17,21-Trihydroxypregna-1,4-diene-3,20-dione
Tetracycline	[4-S-(4-alpha,4a-alpha,5a-alpha,6-beta,12a-alpha)]-4-(Dimethylamino)-

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	1,4,4a,5,5a,6-11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide
Tolnaftate	Methyl-(3-methylphenyl)carbamothioic acid O-2-naphthalenyl ester
Triclosan	5-Chloro-2-(2,4-dichlorophenoxy)phenol
Vitamin A	3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8-nonatetraen-1-ol
Vitamin D	(3-beta,5Z,7E,22E)-9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol
Vitamin E	[2R-2R*(4R*,8R*)]-3,4-Dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-ol
Vitamin K (Phylloquinone)	[R-[R*,R*-(E)]]-2-Methyl-3-(3,7,11,15-tetramethyl-2-hexadecenyl)-1,4-naphthalenedione

The Examiner questioned the inclusion of claims 22 and 23.

Claim 22 was included to specifically and particularly point out examples of the anionic surfactant.

Claim 23 was included to specifically and particularly point out examples of the cationic surfactant.

Rejections Under 35 U.S.C. § 102

The Action rejects claims 1,12-21,25,27, and 28 as being anticipated by Nakajima (5,338,761) which discloses emulsion formulations containing egg or soya lecithin, a non ionic surfactant, cholesterol and an active agent (antibiotic) with the lipid: active agent amounts in the claimed range.

In response, applicants disagree for the following reasons:

- Nakajima describes an emulsion formulation in contrast to applicants' mixed micelle formulation;

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- Nakajima's formulation requires the active agent to be a lipid-soluble drug, in contrast to applicants' active agents, which can be both lipid-soluble and water-soluble;
- Nakajima's formulation has a lipid, a lipid-soluble agent, and a surfactant (phospholipid). In contrast, applicants' formulation has the agent and phospholipid.

In order for a rejection under Section 102 to be sustained, the Federal Court has ruled that, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference" Verdegaal Bros. v. Union Oil Co. of California, 814F. 2d 628,631, 2USPQ 1051,1053 (Fed Cir. 1987).

Pursuant to the standard in Verdegaal, claims 1, 12-21, 25, 27, and 28 are not anticipated by Nakajima because the present invention uses mixed micelles and not emulsions. Therefore, the above rejection should be withdrawn.

Claims 1,5, 12,18, 22, 26, 27, and 29-20 were rejected under section 102 (b) as being anticipated by Pittrof (5,376,646), which discloses mixed micelle compositions containing soya lecithin, antibiotics or anti-inflammatory agents, an antioxidant, polyquaternium, glycholic acid (anionic surfactant), chlorhexidine salts, and sweeteners in a lipid: active agent ratio with the claimed range.

In response, applicants disagree because, even though Pittrof describes mixed micelles, the formulation requires a salt of cholanic acid and a phospholipid. This is because cholanic acid is an essential element required for penetration of the

composition through the skin. Therefore, since the present invention lacks this essential element, it is not anticipated by Pittrof. This rejection should be withdrawn.

Claims 1,5, and 12-30 were rejected under 35 U.S.C § 102 (e) as being anticipated by Schwartz (6,117,415), which discloses oil in water emulsions containing chlorhexidine or triclosan, egg lecithin, triglyceride, alpha-tocopherol hemisuccinate, Tween, peppermint oil, surfactants, and particle size 250 nm to 350 nm.

In response, applicants disagree because claims 1,5, and 12-30 lack an essential element of Schwartz—the oil in water emulsion. Therefore, as a matter of law and fact, this rejection should be withdrawn.

Rejections Under 35 U.S.C. § 103 (a)

Claims 1, 5, 12-18, 22, and 26-30 were rejected as being unpatentable over Pittrof, which does not teach the entire claimed range of lipid to active agent and which uses salts of cholanic acid.

In fact, Pittrof teaches away from the present invention and in no way suggests that the claimed formulation of active agent and phospholipid would have the property of high adhesive capacity to mucosal membranes. What applicants found was an unexpected result—high adhesive capacity to mucosal membranes—and thus applicants' formulation was not obvious under Pittrof. This rejection should be withdrawn under the Graham test, 383 U.S. 1,148 (1966).

Claims 1, 5, and 12-30 were rejected as being unpatentable over Schwartz, which uses an oil in water emulsion and has a polymer that enhances the mucoadhesiveness of the composition. Schwartz neither suggests nor teaches that a

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formulation with no polymer coating and in a mixed micellar form would enhance mucoadhesiveness. What the Examiner has done is apply hindsight in rejecting the above claims. Since hindsight is impermissible under the standard of W.L. Gore & Associates, Inc. v. Garlock Inc, 721 F. 2d 1540 (Fed. Civ. 1983), this rejection should be withdrawn.

Therefore, claims 1, 5, and 12-30 are in condition for allowance and notice to that effect is earnestly solicited. If, for any reason, the Examiner should deem that this application is not in condition for allowance, the Examiner is respectfully requested to telephone the undersigned attorney to resolve and outstanding issues.

Should generic claim 1 and claims 5, 12-30 pertaining to the election of the species disinfectants, be granted, then applicants request that claims 2-4 and 6-11 be reinstated and allowed as indicated by the Examiner (applicant's attorney discussed the restriction by telephone with the Examiner), and in accordance with the terms of the Restriction election made by applicants on October 25, 2001.

Respectfully Submitted,

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